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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/377,081	08/19/1999	PATRICIA GRASSO	19705-001-(A)	7358

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EXAMINER

SAOUD, CHRISTINE J

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 08/26/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/377,081

Applicant(s)

GRASSO et al.

Examiner

Christine Saoud

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jun 9, 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5, 7, 12, 15, 17, 18, 31-33, 43, 44, 46, 47, 49-55, and 57-6 is/are pending in the application.
- 4a) Of the above, claim(s) 5, 43, 44, 46, 47, 49-55, and 57-60 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 7 is/are allowed.
- 6) ☒ Claim(s) 1-3, 12, 15, 17, 18, 31-33, and 61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 4, 6, 8-11, 13-14, 16, 34 and 39 have been canceled, claims 1, 7, 12, 15 and 61 have been amended as requested in the amendment of paper #22, filed 09 June 2003. Claims 1-3, 5, 7, 12, 15, 17-18, 31-33, 43-44, 46-47, 49-55, 57-61 are pending in the instant application.

Election/Restriction

2. Claims 5, 43-44, 46-47, 49-55, and 57-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

Claims 1-3, 7, 12, 15, 17-18, 31-33 and 61 are under consideration in the instant Office action.

Claim Objections

3. Claim 15 and 17 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 15 and 17 broaden the claim from which they depend, claim 7, and are therefore, improper.

4. Claims 31-32 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel

the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 31-32 broaden the claim from which they depend, and are therefore, improper.

Claim Rejections - 35 USC § 112

5. Claims 12, 15, 17, 31-33 and 61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 12, 15, 17, 31-33 and 61 are directed to leptin peptide molecules, wherein the peptides have an amino acid sequence which differs from that of SEQ ID NO:2 and 18 by "consisting essentially of" language, recitations of having conservative amino acid substitutions, having D-amino acids, or variant amino acid substitutions.

Applicant asserts that "homologs, analogs or derivatives" have been deleted from the claims, and therefore, the instant rejection is overcome. This conclusion is not persuasive because the claims still encompass fragments, homologs, analogs and derivatives of the peptides, based on the language indicated above. Therefore, the claims still are directed to a genus of molecules for which a complete structure is lacking in the instant specification. The instant claims encompass peptides which differ from the disclosed purified leptin peptides of SEQ ID NO:2 and 18 by "consisting essentially of" language, recitations of having conservative amino acid substitutions, having D-amino acids, or variant amino acid substitutions. However, the instant specification fails

to provide an adequate written description of any leptin peptides which have an amino acid sequence which differs from that of SEQ ID NO:2 and 18 because no such molecules have been made or tested for their ability to modulate body mass. The instant specification fails to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As the instant claims are directed to subject matter which has yet to be described or isolated, the instant specification lacks a written description of this subject matter, absent evidence to the contrary.

6. Claims 1-3, 12, 15, 17-18, 31-33 and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a leptin fragment comprising the amino acid sequence of SEQ ID NO:2 or 18 (murine and human, respectively), does not reasonably provide enablement for a leptin peptide lacking these amino acid sequences, such as “consisting essentially of”, amino acid substitutions, derivatives, cyclization, or SEQ ID NO:3-10. as recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant contends that the submitted amendments resolve this rejection and that the “specification provides proper and sufficient enabling support for these peptides”. This assertion is not persuasive. As pointed out previously, the specification is only enabling for leptin peptides having a naturally occurring amino acid sequence (SEQ ID NO:2 or 18) because it does not describe the production of any leptin peptide *lacking* that sequence. The specification fails to

describe those molecules, other than the peptides of SEQ ID NO:2 and 18, which have body mass modulating ability. It is noted that SEQ ID NO:3-10 are still claimed, but these peptides are not enabled because there is no evidence indicating that they modulate body mass, and the post filing art of Grasso et al. (Regulatory Peptides, 85: 93-100, 1999) supports this position. Additionally, the pending claims encompass non-naturally occurring mutants of leptin having the disclosed amino acid sequences but does not explicitly identify those amino acid residues which are critical for the biological activity of modulating body mass. For example, claim 15 does not require any amino acid sequence since the claim encompasses an unlimited number of amino acid substitutions. In the absence of guidance, a practitioner of the art of molecular biology would have to resort to a substantial amount of experimental trial and error in the form of deletional and substitutional analysis to identify those critical residues as would be needed to produce a mutant of the disclosed peptides of SEQ ID NO:2 and 18. This trial and error would clearly constitute undue experimentation and, therefore, the instant specification is not enabling for the production of such mutants, which are clearly claimed. The standard for an enabling disclosure is not one of making and testing and the claims constitute a "wish to know". Therefore, the claims are not enabled for their full breadth as outlined above.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 12, 17, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12 and 61 recite “consisting essentially of an amino acid sequence” and “consisting essentially of the amino acid residue sequence”. However, “consisting essentially of” in combination with an amino acid sequence is vague and indefinite because it is not clear what portion of that recited sequence is considered the essential material. There is no clear indication how much of the sequence must be retained, which portion of the sequence will provide for the activity, and what additional amino acids may be added to the recited sequence. Therefore, these claims are vague and indefinite because the metes and bounds cannot be determined.

Claim 17 recites “wherein the conservative amino acid substitutions represent a single amino acid substitution in the mature sequence”. However, there is no antecedent basis for “mature sequence”. In the art, “mature” generally relates to the final processed form a protein, after signal sequence has been removed, post-translational processing has occurred, and the protein has been folded into it’s final biologically active conformation. The peptides of claim 7 are not what one of skill in the art would consider “mature” proteins, but are peptide fragments. Therefore, it is not clear what is intended by the recitation of “mature sequence”, and the claim is indefinite. Additionally, the claim recites “wherein the both the substituted and replacement amino acids are non-cyclic”. It is clear from claim 7 and 15 that the native amino acids are not cyclic, therefore, this recitation regarding the “substituted” amino acid is redundant, and possibly confusing.

Claim Rejections - 35 USC § 102

9. Claims 1-3, 12, 18 and 61 are rejected under 35 U.S.C. 102(a/b) as being anticipated by Grasso et al. (Endocrinol. 138:1413-1418, 1997).

Grasso et al. is of record in the instant application. Grasso et al., at Table 1 on page 1414, disclose leptin peptides, wherein LEP-(116-130) is identical to the instant SEQ ID NO:2 from position 116 to 122. Grasso et al. also teach pharmaceutically acceptable carriers for administration (see "Peptide administration at page 1414). The peptide of Grasso et al. is 15 amino acids long, which meets the limitation of claim 1. The peptide of Grasso et al. consists "essentially of the amino acid sequence" of SEQ ID NO:18, and therefore, meets the limitations of claims 12 and 61. Grasso et al. does not speculate on whether the disclosed peptide binds to the leptin receptor or can cross the blood brain barrier, however, binding activity and transport ability of the peptide would be inherent properties, and therefore, these limitations are also met by the peptide of the prior art, absent evidence to the contrary.

10. Claims 12 and 61 are rejected under 35 U.S.C. 102(a) as being anticipated by Al-Barazanji et al. (WO 97/46585, 12/11/1997).

Al-Barazanji et al. teach leptin peptides, including a peptide which comprises the amino acid sequence of SEQ ID NO:18 (see page 1, lines 35-39), thereby consisting "essentially of the amino acid sequence" of SEQ ID NO:18, wherein the peptides modulate body mass, and therefore, anticipating the instant claims.

Applicant's statements regarding the prior art have been considered. However, the prior art reads on the instant claims for the reasons stated above. Applicant has failed to point out how the claim amendments avoid the prior art of record.

Allowable Subject Matter

11. Claim 7 is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The Examiner can normally be reached on Monday to Thursday from 8AM to 2PM. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §§ 1.6(d) and 1.8). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternate number. Official papers filed After Final rejection filed by fax should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

**CHRISTINE J. SAOUD
PRIMARY EXAMINER**

Christine J. Saoud